With the Author's compl

ON THE VASO-MOTOR NERVES OF THE SMALL INTESTINE.

By J. L. BUNCH, M.D., D.Sc. (Twenty-six Figures in Text.)

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(*From the Physiological Laboratory, University College, London.*)

CONTENTS.

THE circulation in the mesenteric vessels has been investigated, since the researches of Claude Bernard, by numerous observers and by various methods. The simplest method of all, that of direct observation, was made use of by Vulpian[1] to show that stimulation of the mesenteric vessels with the point of a pin causes them to contract, and by Moreau[2] and Budge[3] to prove that stimulation of the splanchnic causes similar constriction.

The effect on the general blood-pressure produced by variations in the intestinal vascular area was investigated by von Bezold and Bensen[4], and by von Basch[5], who showed that the vaso-dilatation of the intestines which was caused by section of the splanchnics produces a fall of general pressure, and that excitation of the peripheral ends of the divided splanchnics causes constriction of the intestinal vessels and rise of general pressure. A similar rise of general blood-pressure was shown by Heidenhain and Grützner[6] to be produced

* The expenses of this research were partly defrayed by a grant from the British Association.

[1] *Comptes rendus de la Soc. de Biol.*, 1858.
[2] *Arch. de Phys.*, IV. 1878.
[3] *Canstatt's Archiv*, 1856.
[4] *Neue Würzburger Zeitung*, 1866.
[5] *Ludwig's Arbeiten*, 1875.
[6] *Pflüger's Archiv*, XVI. 1878.

by excitation of a sensory nerve, and was ascribed by them to constriction of the intestinal vessels.

Asphyxia was proved by Zuntz[1], and by Dastre and Morat[2] to cause constriction of the mesenteric vessels, and the latter asserted that an antagonism exists between the visceral and the cutaneous vessels, so that when the former undergoes constriction the latter dilates.

Dilatation of the intestinal area produced by vaso-dilator nerves has been generally assumed ever since the function of the depressor nerve was known. The fact that section of the splanchnics prevents to a large extent stimulation of the depressor causing a fall of pressure was held to be a proof that these nerves contain vaso-dilator fibres for the intestine, though no direct proof was forthcoming. Dastre and Morat[3], and also Pawlow[4], considered that constriction of cutaneous vessels denotes dilatation of the visceral area, and the former observers found such constriction to occur on stimulation of the depressor. Bradford and Dean[5] also assumed that the fall of blood-pressure which they obtained on stimulating the splanchnic at the rate of 1 per second was due to dilatation of the intestinal area.

The influence of the vagus on the intestinal vessels has been investigated by numerous observers; Rutherford[6] in 1869 stated that stimulation of the peripheral end of the vagus produces no effect on the mesenteric vessels, but Rossbach[7] found that such stimulation causes vaso-constriction. Boehm[8] made a similar statement shortly afterwards, as also have some other observers since.

The results obtained by such methods as direct observation of the intestine or of the mesenteric vessels, and investigation of the changes in general blood-pressure produced by variations in calibre of the intestinal vessels, have been greatly amplified by a plethysmographic method devised by François-Franck and Hallion and published in a valuable paper in the *Archives de Physiologie* for 1896. Not only have these observers been able to confirm many of the results previously obtained, but they have been able to demonstrate to their satisfaction the presence of vaso-dilator fibres in the vagus, and to determine the outflow of vaso-motor nerves to the intestine. Horscraft Waters[9] had previously shown that in the frog the 5th and 6th spinal

[1] *Pflüger's Archiv*, XVII. 1878.
[2] *Arch. de Phys.*, 1882 and 1884.
[3] *loc. cit.*
[4] *Pflüger's Archiv*, XVI. 1878.
[5] This *Journal*, 1889.
[6] *Journ. Anat. and Phys.*, May, 1875.
[7] *Arch. f. Phys.*, 1875.
[8] *Arch. f. exp. Path.*, 1875.
[9] This *Journal*, 1885.

nerves contained vaso-motor fibres for the intestine, and François-Franck and Hallion have now shown that in certain animals, the nature of which however they do not state, the outflow of vaso-motor fibres extends from the 5th dorsal to the 2nd lumbar nerves. These results are however obscured by the adoption of a method, which, though valuable for comparative observations, renders the results difficult of interpretation. Not only are the vaso-motor changes in the intestine recorded on the tracings, but also changes due to movement of the intestine—a factor which is of great importance, since many of the results are obtained by stimulation of nerves which produce contraction or dilatation of the muscular coats of the intestine. I have therefore been led to contrast these results with those obtained by a method which records only the vaso-motor changes of the intestinal vessels. My thanks are due to Professor Schäfer not only for suggesting the research, but also for much valuable assistance and criticism during its progress.

Method.

In this research the plethysmograph has been employed to record the vaso-motor changes of the small intestine. Experiments were first made with an instrument similar to that used by Hallion and François-Franck, the segment of intestine under observation being kept under warm salt solution in a glass vessel connected by means of a tube with a recording tambour[1]. The results obtained by this method were not altogether satisfactory, there being great difficulty in making the apparatus quite tight without unduly constricting the mesenteric vessels, and in most cases cutting off all blood supply to the intestinal segment. A plethysmograph of very simple construction devised by Professor Schäfer has since been employed, consisting of a gutta-percha box with one side of glass, which enables the segment of intestine to be directly observed and the flushing or pallor of the gut to be accurately noted. The mesenteric vessels enter the box on one side through an opening sufficiently large to prevent any pressure being exercised on them, the rest of the aperture being closed by cotton-wool and thick vaseline. The box is connected with a tambour or piston-recorder by an india-rubber tube attached to a glass tube which passes through one side of the box, the whole apparatus being filled with air. A lateral tube leads from this connecting tube, and is closed with a

[1] *Arch. de Phys.*, 1896.

spring clip, so that the pressure within this air-tight system can be raised or lowered at any moment. The intestine is exposed by an abdominal section, the animal in every case being under an anæsthetic, which was varied in different experiments so that any influence due to this cause alone might be discounted by comparative observation. The intestine was kept moist by warm salt solution, and a small segment of intestine having been selected, its mesenteric attachments were divided opposite the two extremities, the gut cut across, and all hæmorrhage stopped. Both ends were left open, and, if necessary, the segment of gut washed out, care being taken to exclude all air from the interior of the segment. The intestine was then placed in the plethysmograph, which was made air-tight with vaseline. The blood supply of the intestine reached it, as a rule, through numerous mesenteric vessels, but in one case only a single artery and vein were left and all nerves passing to it were divided. The tambour was made to record on smoked paper, and the tracing obtained showed most distinctly the alterations in pressure due to respiration and the ventricular beats, the latter being in most cases as well marked as those seen on the blood-pressure tracing taken from the carotid artery. Even in small animals like the rabbit, where the mesenteric vessels are small, the heart-beats are quite plainly seen upon the tracings.

An intestinal vaso-plethysmograph has been described by Edmunds in the *Journal of Physiology* of March 19th, 1898, and used by Halliburton and Mott[1] in their experiments upon the action of choline, etc., which is also constructed of gutta-percha, and closed by a glass plate made tight by vaseline. The shape of the instrument is different from that of the one which I have employed, and a modification of it is also described which is made of metal and has a hot water jacket. In its essential features, however, this plethysmograph is similar to the one which I have made use of since the latter part of 1897.

Effect of Asphyxia on the vaso-motors of the intestine.

Plethysmographic tracings of the small intestine show well-marked heart-beats and respiratory curves, but (when no air is included in the gut) no curves of greater amplitude such as are seen in the case of the spleen and kidney under normal circumstances. It is worthy of attention that the results obtained by François-Franck and Hallion are complicated by contractions of the intestinal walls, as is distinctly

[1] Proc. Physiol. Soc., *Journ. Physiol.* xxii. 1898.

seen in some of their tracings, and this is accounted for by their methods—viz., either tying the ends of the segment of gut under investigation, or introducing into each end a tube which communicates with a tambour. In either case there is a liability to changes in volume of the air included within the gut, and the results obtained must necessarily be difficult of interpretation.

Curves may sometimes be seen on the tracings obtained by the method which I have adopted which correspond with curves present on the carotid pressure tracing. Fig. 1 shows undulations on the

Fig. 1. Traube-Hering curves. ½.

plethysmographic record which correspond accurately with Traube-Hering curves on the blood-pressure tracing. A rise of blood-pressure is seen to be accompanied by constriction of the intestinal vessels, and the succeeding fall of pressure by dilatation of the intestinal vessels. In asphyxia, the first effect is a marked constriction of the vessels of the intestine and an appearance of bloodlessness which may be almost as well defined as that obtained by compression of the thoracic aorta. Compression of the aorta causes a great fall of blood-pressure in the abdominal arteries, accompanied by a marked rise in carotid pressure. This is seen in Fig. 2; when the compression is relaxed the blood-pressure in the intestinal vessels

Fig. 2. Effect on blood-pressure and on intestinal plethysmographic tracing of compression of thoracic aorta. ½.

rises at first rapidly, afterwards more gradually to the normal, and the excursions of the mercury due to the heart-beats are increased

in size, although this would be partly accounted for by the more flaccid condition of the arteries. A similar fall of pressure is obtained by clamping the mesenteric vessels passing to the loop of intestine employed (Fig. 3), but this produces no appreciable effect on the

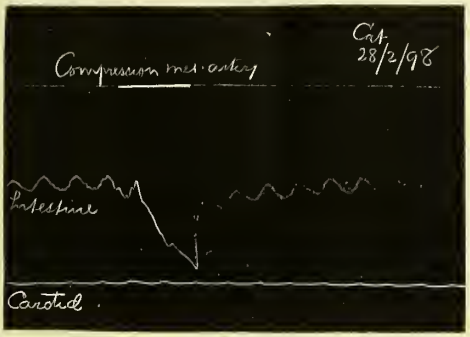

Fig. 3. Effect of compression of mesenteric artery. ½.

general blood-pressure. Asphyxia causes at first an increased force of the cardiac contraction, and constriction of the intestinal vessels which persists for some time. The vessels of the skin dilate, either by reason of a compensatory mechanism which sends the venous blood to the surface, or, as Stefani[1] supposes, owing to a difference in the elastic resistance of the intestinal and superficial vascular systems. Fig. 4 shows that the intestinal vaso-constriction is succeeded by dilatation, although the carotid pressure is rising. This rise of pressure may perhaps be due to constriction of vessels other than those of the intestine, since direct observations of the intestine does not show that its vessels are appreciably constricted. If, however, the intestinal vessels do not dilate during asphyxia, the rise of the plethysmographic curve must be due to passive congestion of the veins. The heart-beats now appear on the plethysmographic tracing larger than before the onset of asphyxia, but this may be merely the result of a diminished rate of beat: ultimately they gradually become less forcible, constriction of the intestinal vessels again sets in, the heart becomes feebler and death ensues. At a temperature of 60° F. death takes place, in a dog anæsthetised with chloroform, 12 to 14 minutes after the onset of asphyxia, in cats rather more quickly, and in rabbits more quickly still. In the latter, however, if the temperature be raised by pouring hot water into the tin on which the animal is placed and

[1] *Atti del XI. Congr. medic. Torino*, 1894, t. II.

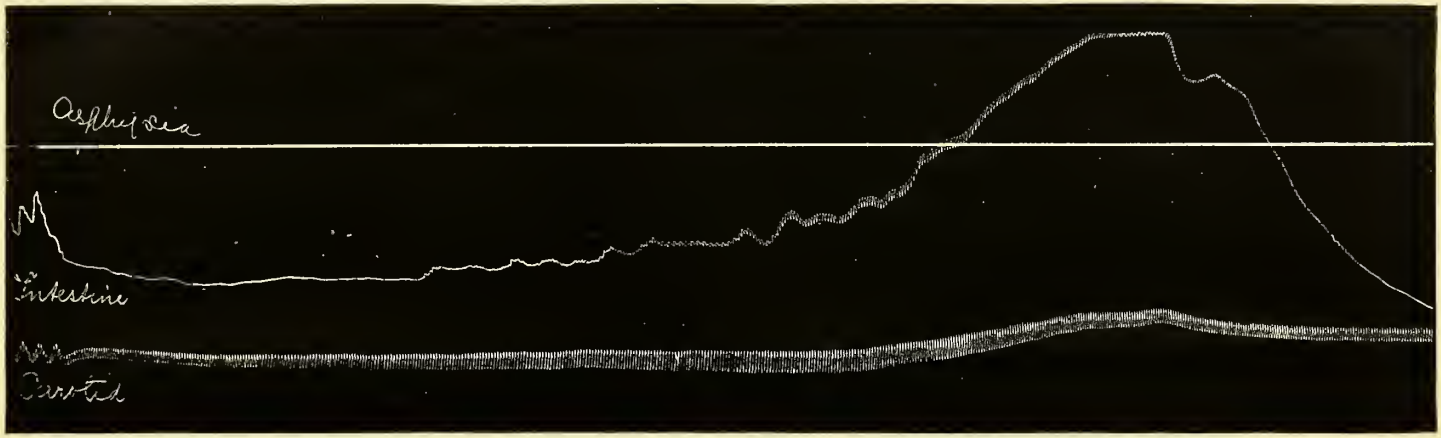

Fig. 4. Dog. Effect of complete occlusion of the trachea. $\frac{1}{3}$.

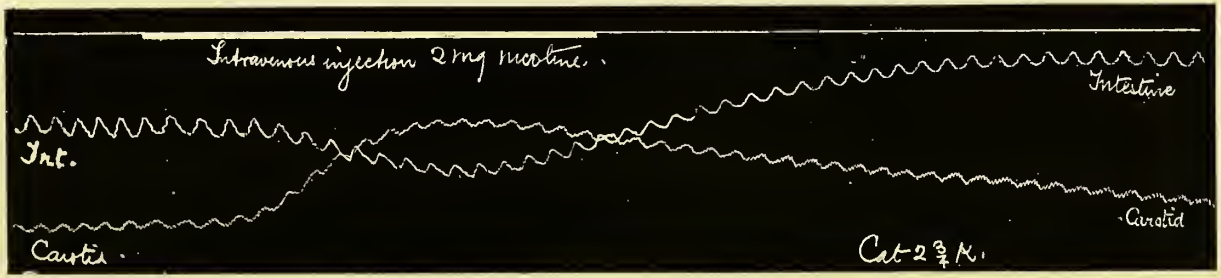

Fig. 5. Effect on intestinal vessels of intravenous injection of nicotine. $\frac{2}{3}$.

artificial respiration be continued, the heart may begin to beat again after it has completely ceased. Richet has even seen spontaneous respiration return under similar circumstances, but in those rabbits with which I have experimented the thorax has been opened and the animal placed under artificial respiration previous to the asphyxia.

Dastre and Morat[1] hold that all the phenomena of asphyxia are phenomena of stimulation, and argue that, since asphyxia causes the pupil to dilate on the side on which the sympathetic is intact while it remains unaffected on the opposite side on which it has been divided, the effect is due to stimulation of a centre in the central nervous system. In asphyxia also, the vaso-constrictor centre for the intestine is first stimulated and later on the vaso-dilator centre if the rise on the plethysmographic curve be not due entirely to passive venous congestion. The continued rise of general pressure, during such vaso-dilatation might be brought about by constriction of those systems, which are affected late in asphyxia.

Effect of drugs upon the vaso-motors of the small intestine.

Of the drugs which have a marked effect upon the small intestine, one of the most powerful is nicotine. Even in minute doses it causes a great constriction of the intestinal vessels synchronous with the rise of general blood-pressure, which is gradually recovered from, and is usually followed by a less marked dilatation (Fig. 5).

In larger doses it causes an enormous effect of the same character, the after-dilatation lasting for a very considerable time and amounting to temporary vaso-motor paralysis, so that if another dose be injected intravenously during this period no effect is produced upon the intestine. In one animal (cat) in which all connections of the portion of intestine in the plethysmograph with the central nervous system had been divided, and in which stimulation of the splanchnic gave passive dilatation of that portion, synchronous with the rise of general blood-pressure, intravenous injection of nicotine caused constriction of the intestinal vessels. This is in accordance with the results of Moore and Row[2], who showed that the action of nicotine is peripheral. In one case an injection of 1 mg. of nicotine caused dilatation instead of constriction of the intestinal vessels (Fig. 6) although accompanied by the usual rise of carotid pressure, and in this case it seems probable

[1] *Arch. de Phys.*, 1884.

[2] This *Journal*, XXII. 1898.

that the peripheral ganglia, or nerve endings, on which nicotine acts had become paralysed, perhaps by the anæsthetic.

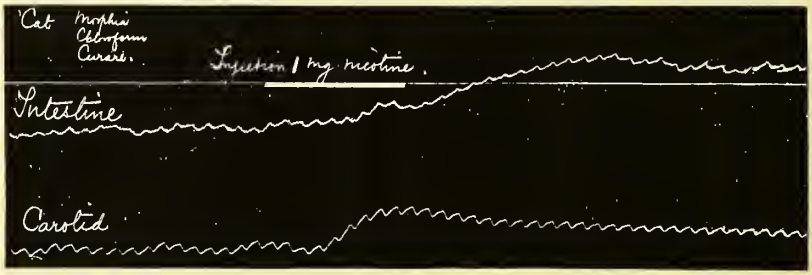

Fig. 6. Unusual effect of injection of nicotine intravenously. Immediate dilatation produced without any preceding constriction. $\frac{2}{3}$.

The action of coniine is similar to nicotine as regards the intestinal vessels, but it produces no after-dilatation and its action is less powerful (Fig. 7).

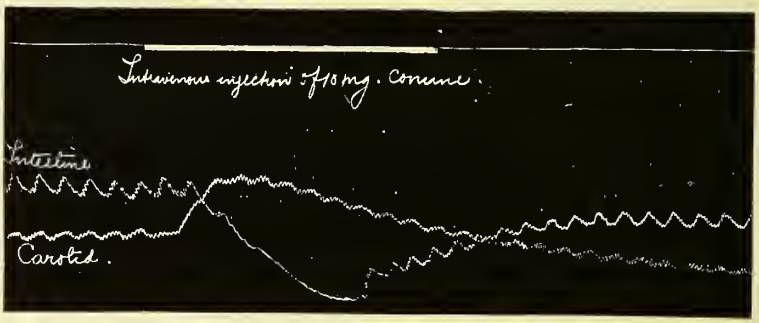

Fig. 7. Cat, 2·75 k. Effect of intravenous injection of coniine. $\frac{1}{2}$.

These tracings were all taken from animals in which both vagi had been divided in the neck, or sufficient atropine had been given to eliminate the action of the vagus on the heart. To avoid the respiratory paralysis caused by the intravenous injection of nicotine and coniine, the animal was placed under artificial respiration.

The effect of the intravenous injection of nicotine on general blood-pressure has been investigated by numerous observers, and Langley and Dickinson[1] have described in detail the vaso-motor effects in the intestine appreciable by direct observation. More recently, Moore and Row[2] have published tracings showing the effect of intravenous

[1] This *Journal*, xi. p. 265. 1892.

[2] This *Journal*, xxii. p. 273. 1898.

injection of nicotine on the kidney volume and on blood-pressure. They find that the rise of pressure produced by the injection is accompanied by considerable constriction of the kidney, which is not followed by any appreciable dilatation. François-Franck and Hallion state that constriction of the kidney may be accompanied by absence of constriction of the intestinal vessels, or even by their dilatation, but in the case of intravenous injection of nicotine, renal constriction is undoubtedly accompanied by diminution of volume of the vessels of the intestine. But nicotine produces an after-effect on the intestinal vascular area different from that on the kidney volume, in that the primary constriction of the mesenteric vessels is followed by marked dilatation, even while the blood-pressure remains considerably raised. As just stated, nicotine does not produce distinct after-dilatation of the kidney. The fact that nicotine may cause dilatation of the mesenteric vessels has already been recorded by Moore and Row in their paper, their results having been obtained by direct observation of the vessels when 1 % solution of nicotine was allowed to flow over them.

I have also investigated the action of piperidine on the vaso-motors of the intestine. The effect is exactly similar to that produced by nicotine and coniine as regards the vaso-constriction it causes, but its action is allied rather to that of coniine, in that it gives rise to no secondary vaso-dilatation. Intravenous injection of neutralised 1 % solution of pyridine on the other hand causes dilatation of the intestinal vessels accompanied by fall of general pressure. The effects of these four drugs on the vaso-motors of the intestine are therefore evidence in favour of the view that the action of nicotine, coniine and piperidine is due to a common cause, probably the presence of a reduced pyridine group[1]. The first injection of pyridine which I administered gave rise to marked constriction of the intestinal vascular area, but the solution of pyridine on examination was found to be strongly alkaline, and it was only on accurately neutralising it that dilatation was obtained. This experiment led me to inject some dilute solution of sodium hydrate into a vein, and it was found to have a vaso-constrictor action on the intestine and to produce rise of carotid pressure[2]. Intravenous injection of normal saline solution was also tried; in small quantities it exerts no perceptible effect upon the intestinal vessels. The entry of sodium sulphate solution into the circulation frequently sets up a series of extensive curves on the

[1] Cf. Moore and Row, *loc. cit.*

[2] Cf. Gaskell. *Roy. Soc. Proc.* 30, 1880, pp. 225–227.

plethysmographic tracing, which correspond with the curves of a Traube-Hering character seen on the carotid pressure tracing under such circumstances. The curves are indistinguishable from those shown in Fig. 1.

Injection of extract of mammalian suprarenal causes very great vaso-constriction of the intestinal area.

The effect of alcohol on the circulation was investigated by Hering, who found that it slows the circulation, since potassium prussiate injected into the circulation of a horse completes the circuit normally in 30 seconds, but takes 40 seconds after the alcohol has been injected. Zimmerberg[2] showed that alcohol lowers blood-pressure and causes diminution of the cardiac contractions. Marvaud[3] found that it lowers the pressure in man when given in doses of 20—50 grammes of brandy. Dilute solutions of alcohol even as strong as 40 % do not produce any distinct effect on the intestinal vessels when injected intravenously, although, as one might expect, absolute alcohol when injected undiluted does produce vaso-constriction.

Eserine causes a rise of carotid pressure, and a very marked constriction of the vessels of the intestine (Fig. 8).

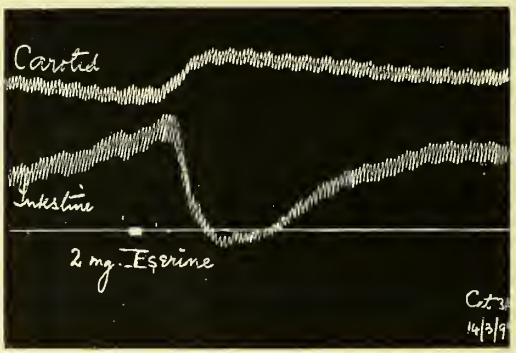

Fig. 8. Cat, 3k. Effect of injecting 2 mg. eserine intravenously. ½.

Ergotine, when injected intravenously, causes a slight preliminary dilatation of the intestinal vessels, which is succeeded by constriction, and later on by still more marked dilatation. The intestinal vaso-constriction is accompanied by contraction of the circular coat of the

[1] *Diss. inaug.*, Dorpat, 1869.
[2] *L'alcool, son action physiologique*, Paris, 1872.

intestine (Fig. 9). After a slight preliminary rise, the carotid pressure falls in spite of the constriction of the intestinal vessels, probably from direct action of ergotine on the heart.

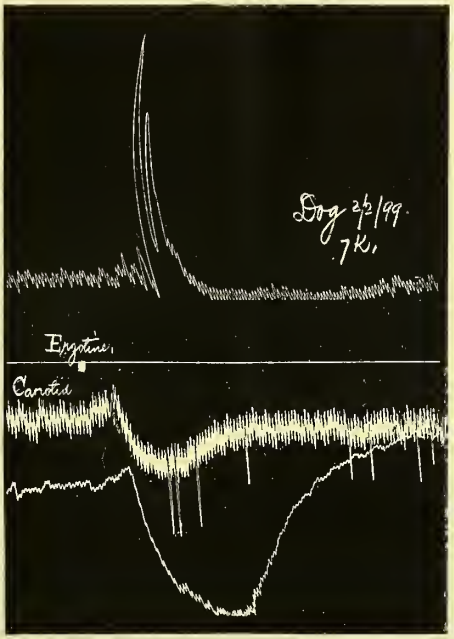

Fig. 9. Intravenous injection of 2 mg. ergotine. The uppermost curve shows the effect upon the circular coat of the intestine, as obtained by inserting a small india-rubber bag containing fluid. The lowermost curve is that of the intestinal vessels.

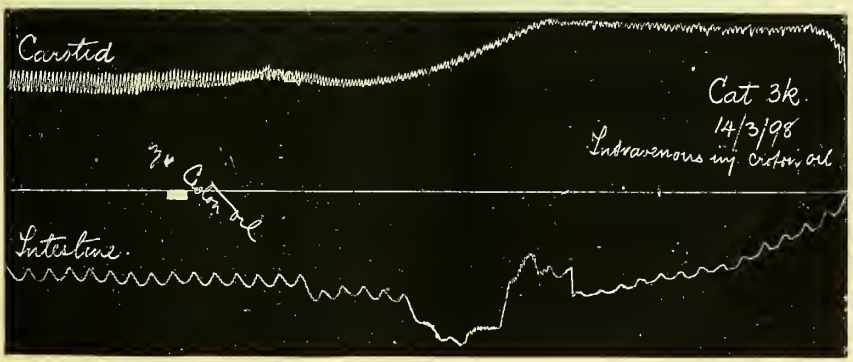

Fig. 10. Effect of injection of croton oil. ½.

The intravenous injection of croton oil (Fig. 10) causes a rise of blood-pressure, and a primary constriction of the intestinal vessels, followed by dilatation. Whether its cathartic action is to any appreciable extent dependent on its vascular effects, there is not sufficient evidence to show, but it is worthy of note that many other drugs which cause systolic tone of the intestine, such as nicotine, also have a vaso-constrictor action on the intestinal vascular area.

Influence of various Nerves.

The influence of the splanchnic on the mesenteric vessels was investigated long ago by the method of direct observation, and recently François-Franck and Hallion[1] have stimulated the sympathetic cord within the thorax, and also the rami communicantes, and have recorded the results by means of their plethysmograph. Nowhere in their paper is it stated that reflex effects were guarded against by division of the rami communicantes on the proximal side of the point of stimulation. Even assuming that this precaution was taken, the effects on the intestinal walls, which I have elsewhere[2] shown to be produced by splanchnic stimulation, would have to be taken into con-

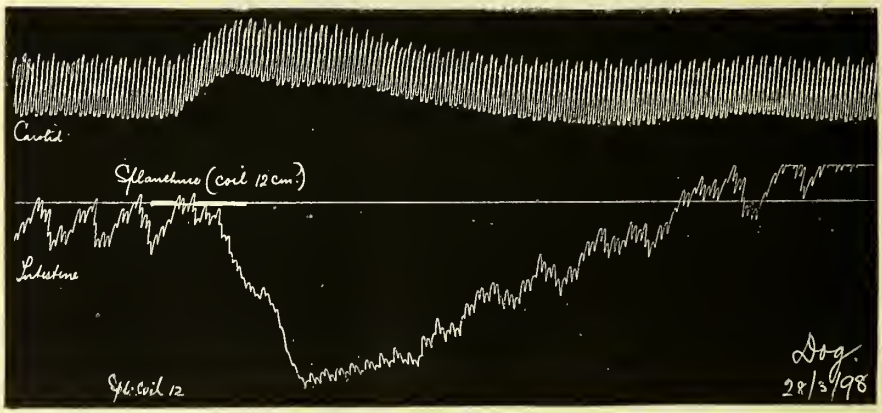

Fig. 11. Dog. Effect on intestinal vessels of stimulating the splanchnic. An after-dilatation is seen beyond the power of the tambour to record. $\frac{1}{3}$.

sideration when interpreting the authors' results. They do not state that they have stimulated the peripheral end of the divided splanchnic

[1] *loc. cit.* [2] This *Journal*, 1898.

and recorded the effect on the intestinal vessels. This experiment I have performed on rabbits, cats and dogs, precautions being taken to avoid the reflex effects which may complicate the result unless the branch which the greater splanchnic receives from the lesser splanchnic be divided. The splanchnic was stimulated on both sides, at different levels, with different rates of repetition of the stimulus, and with different strengths of current. In almost every case I have found such stimulation to produce a rise of blood-pressure accompanied by constriction of the intestinal vessels and followed by more or less well-defined dilatation (Fig. 11). Even when this after-dilatation is well-marked, there is no corresponding fall of general pressure below the normal; indeed, the general blood-pressure normally remains somewhat raised.

Pure vaso-dilatation was not always produced by stimulation of the splanchnic with weak currents or with slowly repeated stimuli at the rate of 1 per second, or even less, but in a few cases I have succeeded in obtaining it. Fig. 12 shows dilatation of the intestinal vessels

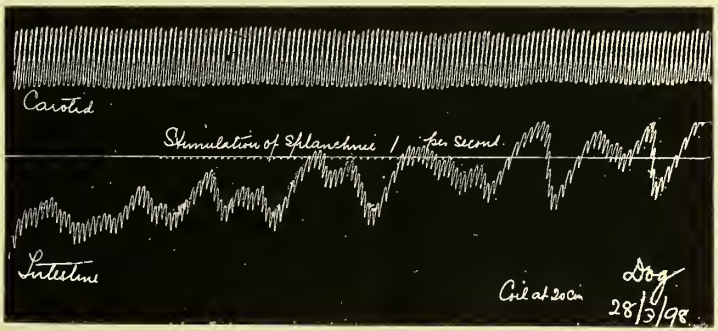

Fig. 12. Dilatation of the vessels of the intestinal segment produced by stimulation of the peripheral end of the divided splanchnic. No effect on general blood-pressure.

obtained by stimulating the peripheral end of the splanchnic with very weak and slowly repeated stimuli. The effect is unaccompanied by any rise of general blood-pressure and the dilatation may therefore be considered an active one, as distinguished from vaso-dilatation which is accompanied by a rise of general pressure. In a few experiments the arterial cannula was connected with a mercury-valve, or regulator[1], of rather large bore, sufficiently wide to enable the blood to escape freely

[1] Cf. Bayliss, This *Journal*, xxiii. Supp. p. 14, 1898.

when any rise of pressure took place in the carotid artery, and thus maintain the general blood-pressure at a constant level. Fig. 13 shows

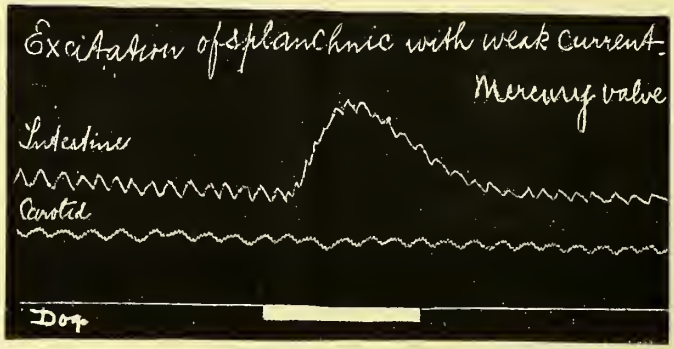

Fig. 13. Dog. Dilatation of intestinal vessels on stimulation of peripheral end of cut splanchnic. General blood-pressure maintained constant by means of mercury regulator.

the effect obtained in a dog on stimulation of the peripheral end of the splanchnic with the coil at 12 cm., intestinal vaso-dilatation taking place apart from any general rise of blood-pressure. When obtained, this dilator effect of the splanchnic is abolished by doses of nicotine such as are capable of abolishing the constrictor effect of the splanchnic. In one case I succeeded in dividing all nerves accompanying the one mesenteric artery which connected the segment of intestine with the general circulation, and in this case excitation of the splanchnic caused passive dilatation of the vessels of the isolated loop along with the rise of general blood-pressure (Fig. 14).

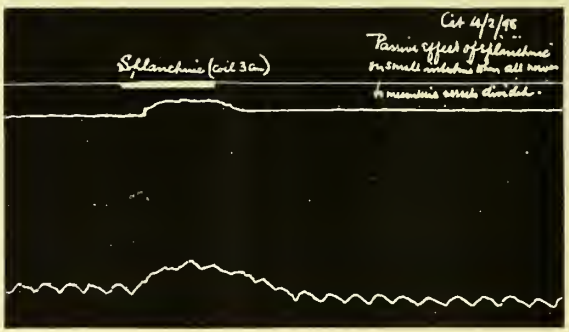

Fig. 14. Passive effect of stimulating splanchnic; all nerves to intestinal segment divided. $\frac{1}{2}$.

The vagus has been stated by François-Franck and Hallion[1] to produce vaso-dilatation of the intestine whether stimulated in the thorax without atropine, or in the neck after administration of atropine. No statement is made as to the nature of the animals in which these results were obtained. In the rabbit and in the cat I have been unsuccessful in obtaining such results, and only in one dog did excitation of the peripheral end of the vagus produce vaso-dilatation (Fig. 15).

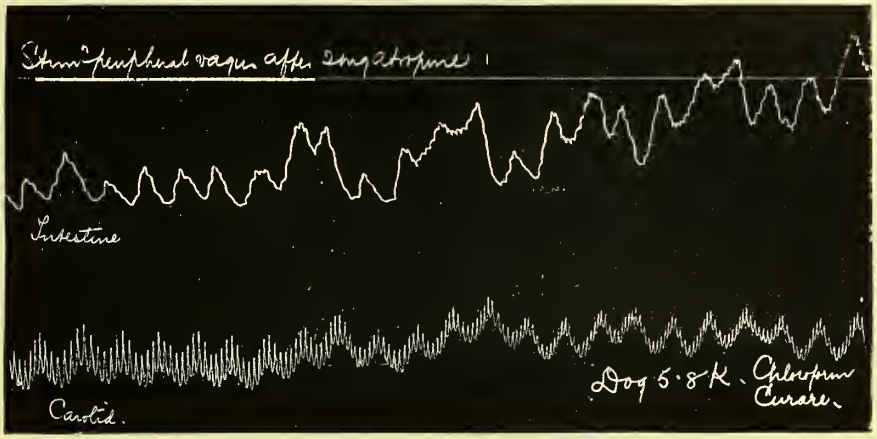

Fig. 15. Unusual effect obtained in one dog by excitation of the vagus. Dilatation of the intestinal vessels could not be made out by direct observation of the intestine. $\frac{2}{3}$.

In this case the vagus was stimulated in the neck after the administration of 2 mg. of atropine, and some vaso-dilatation followed the shutting

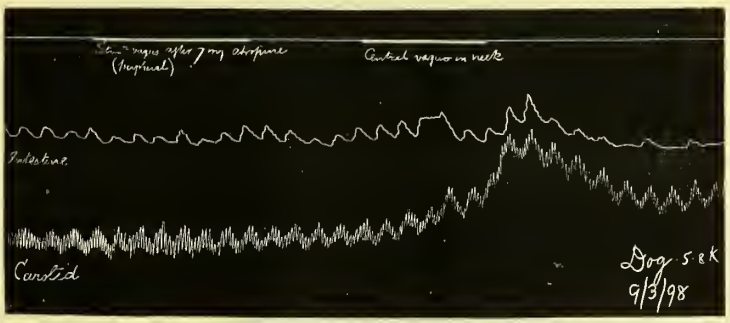

Fig. 16. Dog, 5·8 k. Effect of stimulating the vagus in the neck after the injection of 7 mg. atropine. $\frac{1}{3}$.

[1] *loc. cit.*

off of the current, accompanied by a slight diminution in the size of the heart-beats. Another 5 mg. of atropine was then injected, but stimulation of the peripheral end of the vagus now produced no effect, although stimulation of the central end still gave the usual result (Fig. 16).

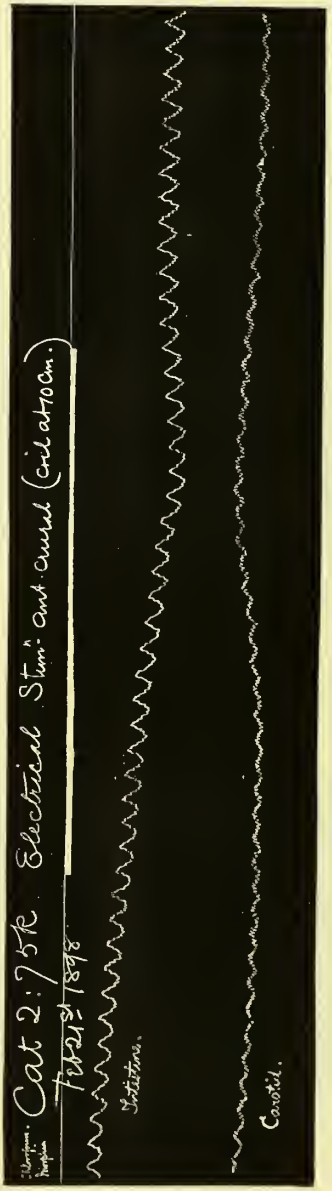

Fig. 17. Stimulation of the central end of the divided anterior crural nerve. $\frac{2}{3}$.

François-Franck and Hallion however state that they have obtained vaso-dilatation on exciting the cervical vagus after the administration of as much as 25 mg. of atropine, although in their published tracing such dilatation appears only as an after-effect. Rossbach[1] has also described vaso-motor effects as being obtained on excitation of the vagus, but he states that they are abolished by atropine in doses greater than 4 mg., no effect on general blood-pressure being obtained after injection of quantities in excess of this.

Stimulation of the peripheral end of the cervical vagus when no atropine has been injected causes a fall of blood-pressure both in the general and intestinal systems.

Lovèn, Grützner and Heidenhain, and others have shown that stimulation of the central end of certain sensory nerves causes rise of general pressure, and Fig. 17 proves that constriction of the intestinal area accompanies such rise of pressure, and must contribute largely towards it. In the rabbit, however, when anæsthetised by chloroform. I find that excitation of the central end of the anterior crural nerve causes dilatation of the intestinal area instead of constriction. Bayliss[2] supposes that the nerves of the limbs in the rabbit contain depressor as well as pressor fibres, the former only producing an

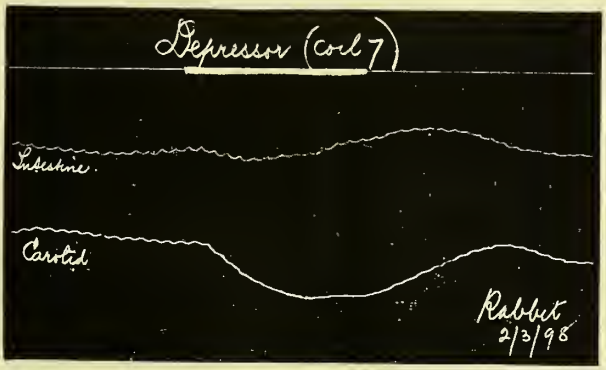

Fig. 18. Rabbit. Excitation of depressor nerve.

appreciable effect when the vaso-constrictor centre is paralysed by chloroform. This is then also true for the nerves of the intestine.

[1] *Arch. f. Phys.*, 1875, p. 439.
[2] This *Journal*, 1893.

Dilatation of the intestinal area has long been assumed to be produced by excitation of the depressor in the rabbit, and this is shown to be the case in Fig. 18, the fall of pressure being accompanied by dilatation of the intestinal vessels. In the cat I have also succeeded in stimulating corresponding fibres, the excitation of which produces intestinal vaso-dilatation exactly comparable to that obtained on stimulation of the depressor in the rabbit.

In the dog, stimulation of the central end of the divided vagus sometimes produces a similar intestinal vaso-dilatation, which is how-

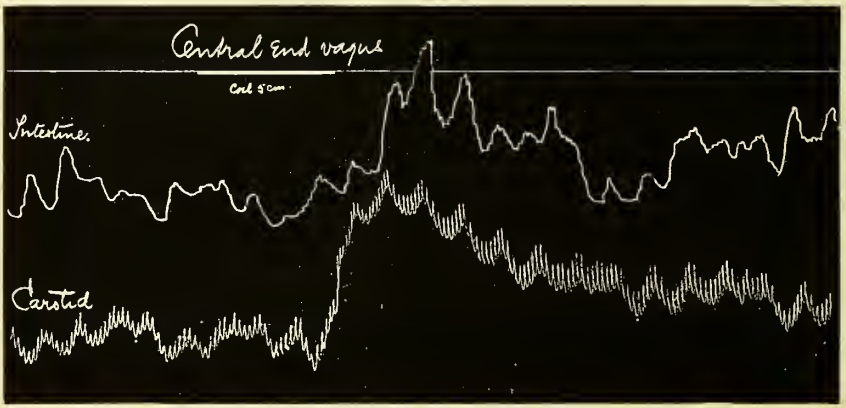

Fig. 19. Dog. Stimulation of vagus. $\frac{2}{3}$.

ever accompanied by a rise of general pressure instead of a fall (Fig. 19). Vaso-constriction must therefore take place to a marked degree in

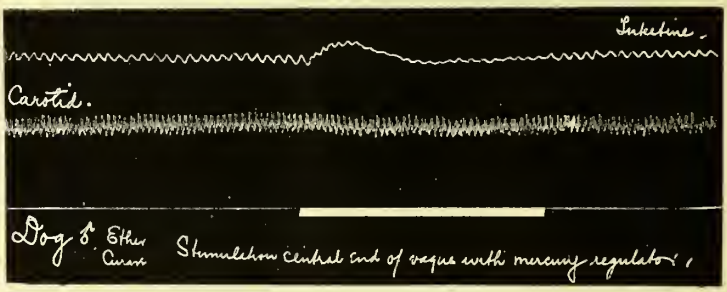

Fig. 20. Dog. Dilatation of intestinal vessels produced by stimulation of the central end of the thoracic vagus. General blood-pressure maintained constant by means of mercury regulator.

some area other than the small intestine. This intestinal vaso-dilatation is also obtained on stimulation of the central end of the cut vagus when the arterial cannula is connected with a mercury regulator, so as to avoid any general rise of blood-pressure (Fig. 20), but I failed to obtain it when both splanchnics were divided. In these experiments on afferent nerves, both vagi were divided, so as to avoid reflex cardiac inhibition.

On the vaso-motor outflow from the spinal cord.

Having succeeded in demonstrating the presence in the splanchnic of both vaso-constrictor and vaso-dilator fibres for the small intestine, some experiments were performed in order to determine, if possible, the origin of these fibres from the spinal cord. As Bradford[1] has shown that the renal vaso-motors pass out through the anterior roots of the 4th dorsal to the 2nd lumbar nerves, slight vaso-motor effects being obtained even on excitation of the 3rd and 4th lumbar roots, it seemed probable that the vaso-motor nerves to the small intestine would have an origin from the spinal cord as least as extensive as this. The investigation was therefore directed to the whole of the dorsal and the upper lumbar roots, the method adopted being similar to that made use of in the case of the viscero-motor fibres of the small intestine[2]. The nerve-roots having been exposed as they passed outwards to the intervertebral foramina were tied with threads of different colours and divided centrally to the ligature, the corresponding segment of spinal cord being also removed so as to avoid any possibility of spreading of the current to it. The nerve-roots were stimulated from above down with faradic currents of different strengths and with various rates of repetition of the stimulus. It has been suggested that, when using strong currents, there is a possibility of the current spreading to some slight extent to fibres arising from roots other than the one stimulated by means of the sympathetic chain, which forms a longitudinal connection between these fibres. Such is however not the case to any appreciable extent, since the excitation of certain nerve-roots causes a much greater effect both on the vessels of the intestine and on the general blood-pressure than does the stimulation of nerve-

[1] This *Journal*, x. p. 358. 1889.
[2] This *Journal*, xxii. p. 357. 1898.

roots either higher or lower than these. In the *dog*, vaso-constrictor fibres to the small intestine pass out in the 4th to the 16th post-cervical nerve-roots, the greatest effect being obtained on stimulating the 10th to the 14th. Fig. 21 shows the effect in a dog of stimulating

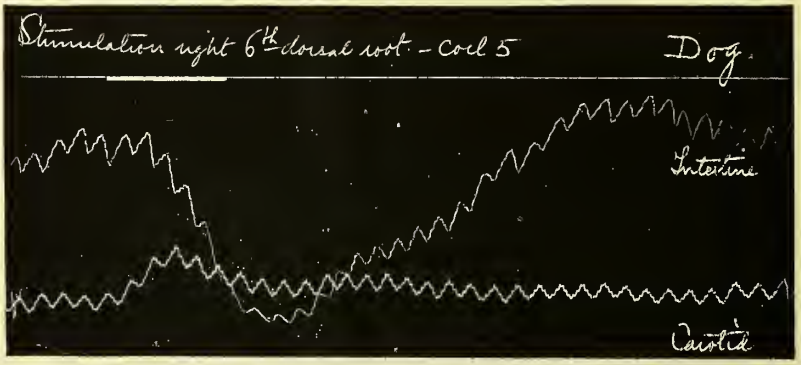

Fig. 21. Dog. Effect of stimulating 6th dorsal nerve-root.

the 6th dorsal nerve-root. Some vaso-constrictor fibres appear also to pass out in the 2nd and 3rd post-cervical roots, but the effect is less than that obtained with the 4th.

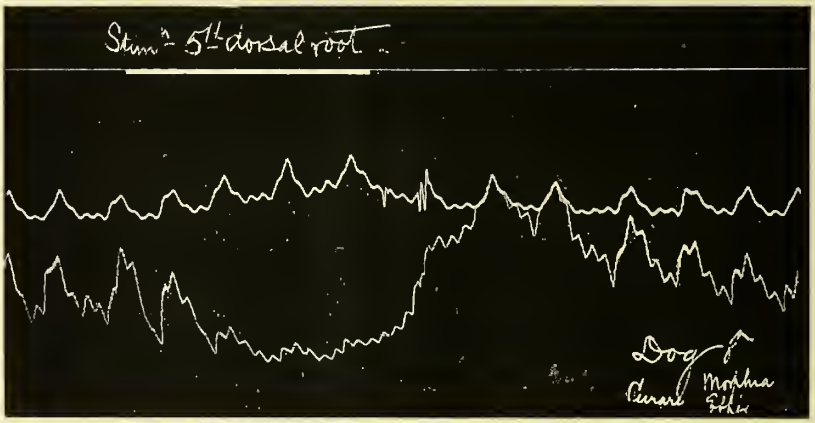

Fig. 22. Dog. Stimulation of 5th dorsal root. Coil at 10 cm.

When employing a current of moderate intensity the vaso-constrictor effect was sometimes followed by dilatation (Fig. 22), and this was still

more noticeable when a weak current was used. The dilatation lasted usually a considerably shorter time than the vaso-constriction, and the plethysmographic tracing quickly returned to normal. Pure vaso-dilatation was obtained in some cases, and most easily in the case of the 2nd and 3rd post-cervical roots, when the constrictor fibres appear to be much less numerous (Fig. 23). Stimulation of these roots with a weak current caused an immediate rise of the lever connected with the

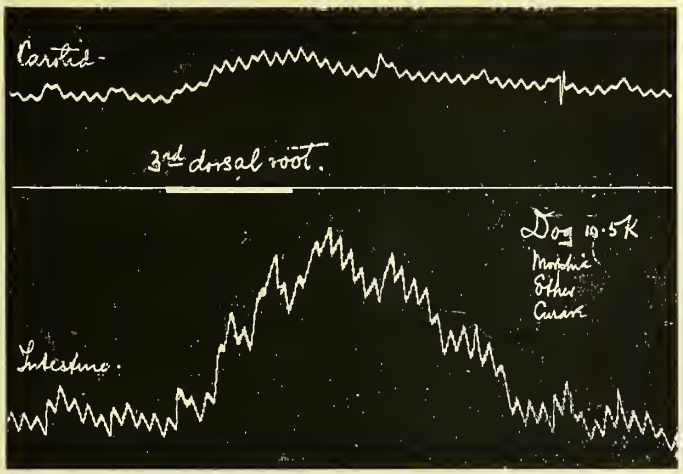

Fig. 23. Dog. Stimulation of 3rd dorsal root. Coil at 10 cm.

plethysmograph, and in estimating the effect it must be remembered that a piston-recorder was employed which was certainly sensitive but which did not greatly magnify the results. In these experiments the carotid blood-pressure was also recorded, so as to obviate any possibility of confusing a merely passive congestion of the intestine with an active and true expansion.

An attempt was made to determine whether the vaso-motor innervation was in any way segmental, by taking two segments of small intestine, one near the pylorus and the other near the ileo-cœcal valve and observing simultaneously the effects produced on them by excitation of nerve-roots. Only two experiments were successful, but these did not tend to show that the innervation of the two segments was appreciably different.

In the *cat*, the severity of the operation and the susceptibility of

the animal to drugs rendered the method of stimulating the divided anterior roots of the spinal nerves extremely difficult. The less severe method of exposing a short segment of spinal cord, dividing it above and below, and inserting needle electrodes, one into the upper and one into the lower end of the segment, has given more satisfactory results. When a current is sent through such a segment, the effect produced on the intestinal vessels may be of such a character that dilatation is more marked than constriction when the current is not strong, constriction becoming more evident as the strength of the current is increased. Thus, in Fig. 24, where the segment of spinal cord extended

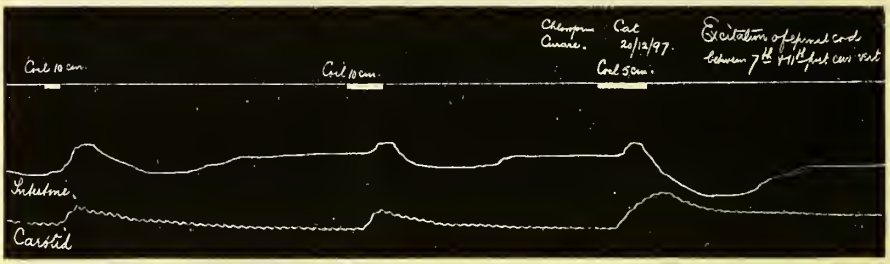

Fig. 24. Cat. Stimulation of segment of spinal cord between the 7th and 11th dorsal nerve-roots.

from the lower level of the 7th to the lower level of the 11th post-cervical vertebræ, vaso-constriction was very slightly marked with the coil at 10 cm., but well marked with the coil at 5 cm., and still more so with the coil home. The tracing is unusual inasmuch as the constrictor effect follows the dilator effect, a result which I have not succeeded in obtaining by excitation of the splanchnic.

In two cases in the cat the splanchnic was exposed on one side as well, and small doses of nicotine injected, until stimulation either of the spinal cord or of the splanchnic failed to produce an effect. In both these cases, however, an amount of nicotine sufficient to abolish the effect of one had a similar effect on both, the effect of stimulation disappearing simultaneously in the cord and splanchnic. These two experiments therefore support the view of Langley[1], that there is only one cell station interposed in the course of the fibres passing to the vessels from the spinal cord, and that this is peripheral to

[1] *A Short Account of the Sympathetic System*, 1895.

ganglia of the sympathetic chain. They are also in accordance with the results which I have previously obtained in the case of the intestinal viscero-motor fibres.

Summary of Conclusions.

1. The vessels of the small intestine are supplied both by vaso-constrictor and by vaso-dilator fibres, which reach the intestine chiefly, if not entirely, by the splanchnic nerves.

2. Variations in calibre of the intestinal vessels may occur during asphyxia which do not correspond to changes in the general arterial system. Thus, the general rise of pressure may, during certain stages of asphyxia, be accompanied by dilatation either of the intestinal arteries or veins.

3. Nicotine causes great constriction of the intestinal area, synchronous with the rise of general blood-pressure; this is gradually recovered from and is followed by a less marked dilatation. In large doses, nicotine causes an enormous effect of the same character, the after-dilatation lasting for a very considerable time and amounting to temporary vaso-motor paralysis.

4. Coniine and piperidine have an action on the intestine similar to that of nicotine but pyridine causes intestinal vaso-dilatation.

5. Stimulation of the peripheral end of the cut splanchnic causes vaso-constriction of the intestinal area, which is followed by more or less well-defined dilatation. When excited with weak and slowly repeated stimuli, dilatation only may be produced.

6. The splanchnic, therefore, contains both vaso-constrictor and vaso-dilator fibres for the small intestine, the vaso-constrictor fibres being probably the more numerous, or, at least, the more powerful.

7. Stimulation of the peripheral end of the cut vagus, whether in the thorax without atropine, or in the neck after the administration of small doses of atropine, causes no vaso-motor effect on the vessels of the small intestine. This is true for the dog, cat and rabbit.

8. Vaso-motor fibres for the small intestine of the dog leave the spinal cord by the anterior roots of the 2nd to the 16th post-cervical nerves. The higher roots contain more dilator, the lower more constrictor fibres.

9. The vaso-motor fibres passing to the small intestine have a cell-station between the ganglia of the sympathetic chain and the mesenteric nerves.

Addendum. February 1st, 1899.

It has recently been shown by Bayliss and Starling[1] that repeated excitation of the vagus in the dog, especially with strong currents, gives rise to increased contractions of the small intestine. I have, therefore, carried out some experiments in order to determine whether such repeated stimulation can also give rise to vaso-motor

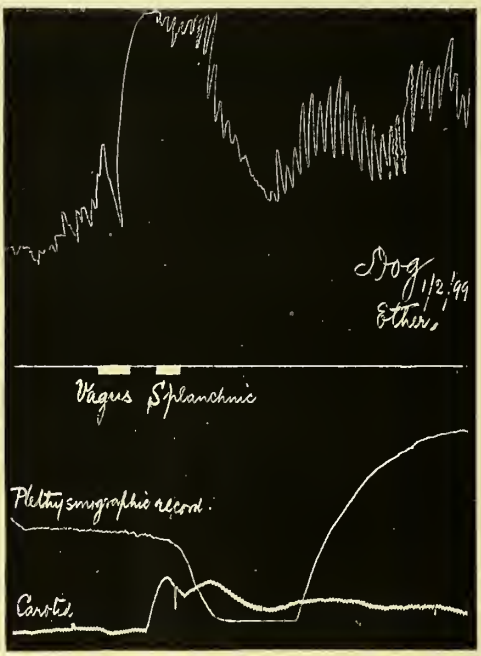

Fig. 25. Effect produced upon the circular coat and the vessels of the small intestine by stimulating successively the thoracic vagus and the splanchnic with the same strength of current.

effects on the small intestine. A small rubber bag filled with fluid was inserted in a loop of intestine, and a segment of small

[1] This *Journal*, xxiii., No. 5.

intestine some distance away was placed in the plethysmograph, and the peripheral end of the thoracic vagus stimulated repeatedly until increased contractions of the intestine were set up. These contractions are as a rule preceded by a short stage of inhibition, and it seems that when once they have been produced by excitation of one vagus, stimulation of the other vagus is equally capable of producing them, even though it has not previously been stimulated. Unless the current used is sufficiently strong to spread to the splanchnic, such excitation does not produce any effect upon the vessels of the small intestine, as recorded by the plethysmograph, nor upon the general blood-pressure. In Fig. 25, stimulation of the peripheral end of the cut intrathoracic vagus caused great contraction of the circular coat of the intestine, but

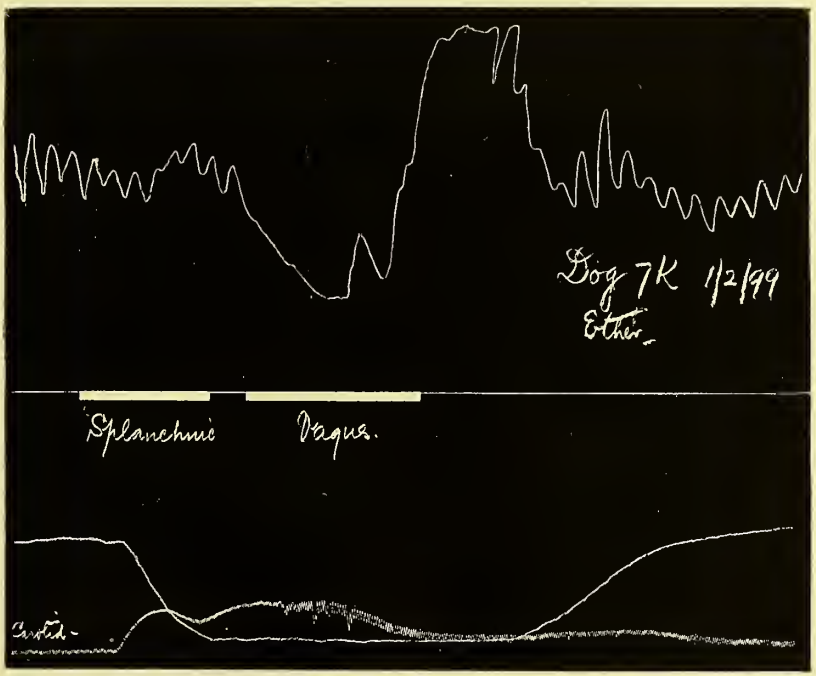

Fig. 26. Successive stimulation of splanchnic and thoracic vagus. Coil at 8 cm. The upper tracing records contractions of the circular coat, the lower carotid blood-pressure.

no effect was produced upon the intestinal vessels until the splanchnic was stimulated.

It is noticeable in the tracing that although the splanchnic stimulation was sufficient to cause a marked effect both upon the general blood-pressure and upon the vessels of the small intestine, it did not inhibit the contraction of the circular coat. This absence of inhibition is also shown in Fig. 26, where excitation of the splanchnic caused slight contraction of the circular coat. Stimulation of the vagus immediately afterwards produced first inhibition of this contraction, followed by a still more considerable contraction. These two tracings tend to show that alterations in calibre of the circular coat are not dependent on alterations in calibre of the intestinal vessels.